Appendix B
A Marked Up Copy Of The Amended Claims To Show Changes.

56. (Amended) A substrate for analyzing a nucleic acid, the substrate comprising:

a cavitated fiber optic [surface; and a nucleic acid sequence linked to the fiber optic surface] wafer formed from a fused bundle of a plurality of individual optical fibers, each individual optical fiber having a diameter between 3 and 100 μm, the wafer comprising a top surface and a bottom surface, the top surface comprising at least 10,000 wells, wherein said wells are etched into the top surface of the cavitated fiber optic wafer and wherein the thickness of the wafer between the top surface and the bottom surface is between 0.5 mm and 5.0 mm in thickness; and wherein the depth of each well ranges from between one half the diameter of an individual optical fiber to three times the diameter of an individual optical fiber;

a plurality of beads within the cavitated wafer, wherein each bead has a pyrophosphate sequencing reagent attached thereto.

64. (Amended) [A] The substrate [with a cavitated surface comprising] of claim 56 wherein the wafer further comprises 10^3 or more groups of oligonucleotides [attached to the surface in discrete known regions, the 10^3 or more groups of oligonucleotides occupying a total area of less than 1 cm^2 on said substrate, said groups of oligonucleotides having different nucleotides] in said wells.

69. (Amended) An array of more than 1,000 different groups of oligonucleotide molecules [with known sequences covalently coupled to a surface of a cavitated substrate, said groups of oligonucleotide molecules each in discrete known regions and differing from other groups of oligonucleotide molecules in monomer sequence, each of said discrete known regions being an area of less than about 0.01 cm^2 and each discrete known region comprising oligonucleotides of known sequence, said different groups occupying a total area of less than 1 cm^2] comprising a cavitated fiber optic wafer formed from a fused bundle of a plurality of individual optical fibers, each individual optical fiber having a diameter between 3 and 100 μm, the wafer comprising a top surface and a bottom surface, the top surface comprising at least 10,000 wells, wherein said wells are

etched into the top surface of the cavitated fiber optic wafer and wherein the thickness of the wafer between the top surface and the bottom surface is between 0.5 mm and 5.0 mm in thickness; and wherein the depth of each well ranges from between one half the diameter of an individual optical fiber to three times the diameter of an individual optical fiber.

84. (Amended) An apparatus for processing a plurality of [analytes] nucleic acids, the apparatus comprising:

a flow chamber having disposed therein a [substrate comprising a plurality of cavitated surfaces, said cavitated surfaces having disposed thereon nucleic acid molecules] cavitated fiber optic wafer surface

[a flow chamber having disposed therein a;]

a cavitated fiber optic wafer formed from a fused bundle of a plurality of individual optical fibers, each individual optical fiber having a diameter between 3 and 100 μm, the wafer comprising a top surface and a bottom surface, the top surface comprising at least 10,000 wells, wherein said wells are etched into the top surface of the cavitated fiber optic wafer and wherein the thickness of the wafer between the top surface and the bottom surface is between 0.5 mm and 5.0 mm in thickness; and wherein the depth of each well ranges from between one half the diameter of an individual optical fiber to three times the diameter of an individual optical fiber;

a plurality of beads within the cavitated wafer, wherein each bead has a pyrophosphate sequencing reagent attached thereto;

fluid means for delivering [processing] pyrosequencing reagents from one or more reservoirs to the flow chamber so that [the analytes anchored to the plurality of microparticles] nucleic acids disposed in the wells of the fiber optic wafer are exposed to the reagents; and

detection means for detecting [a sequence of optical signals from each microparticle of the plurality, each optical signal of the sequence being indicative of an interaction between a processing reagent and the analyte anchored thereto, wherein said detection means is in communication with the cavitated surfaces] optical signals from each well, wherein said detection means is in communication with the wells, each optical

signal being indicative of reaction of the pyrosequencing reagents with the nucleic acid in a well.

86. (Amended) The apparatus of claim 8[7]5, wherein said detection means is a CCD camera.